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Advanced Algorithms for Rapidly Reconstructing Clandestine Releases of Biological Agents in Urban Areas

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Final Report on LDRD Project 99-ERD-069

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Health and Ecological Assessment Division
Earth & Environmental Sciences Directorate
University of California
Lawrence Livermore National Laboratory
P.O. Box 808, L–286
Livermore, CA 94551-0808
Voice: 925-422-3840; FAX: 925-423-6785; GISCenter@llnl.gov

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SUMMARY

As the United States enters the 21st Century it has transitioned out of the Cold War to be the preeminent global peacekeeper and international defender of human rights and democratic principles. As a consequence of this political and military posture, there is an increasing likelihood that the United States will be the target of acts of terrorism. Of greatest concern is that such acts of terrorism might involve the use of weapons of mass destruction (WMD), most notably chemical- or biological-warfare agents, because such acts could produce great attention, widespread fear, and significant loss of life.

Because biological agents can be relatively low-cost, low-technology weapons that can produce more harm to people than to infrastructure, potential aggressor nations, terrorist groups, and even malicious individuals can develop capabilities for covertly manufacturing, transporting, and using them for acts of terrorism. Additionally, the use of a biological agent in an act of terrorism may be more destructive, attract wider attention, and generate greater fear than any chemical agent that might otherwise be employed [see Siegrist (1999) and Stern (1999)][*]. These considerations, along with evidence that terrorists increasingly are targeting civilian populations—in order to inflict indiscriminate casualties—as well as other more traditional targets, such as symbolic buildings or organizations (see Tucker, 1999)[*], suggest that developing a capability for rapid treatment after a biological event may be more practical than concentrating on prevention (see Siegrist, 1999)[*], especially when sensors that can detect a covert event are unlikely to be deployed in every populated location. In fact, Kaufman et al. (1997)[†] even provide a convincing economic argument that developing the capability to provide rapid treatment to victims after a biological incident may save more lives and more effectively limit costs than investing substantial resources in developing methods for preventing such an event. Consequently, there is a critical need for a rapid assessment and evaluation system that will significantly improve the first-response of law enforcement, emergency medical providers, and recovery managers to a covert undetected biological event (CUBE) in an urban environment.

The approach for this exploratory research project was to first select a hypothetical, but plausible, CUBE scenario—a terrorist release of *Bacillus anthracis* (i.e., anthrax) spores into the atmosphere of an urban environment. Then, a system architecture and a set of advanced algorithms was developed to demonstrate that a web-accessible custom GIS application could be used successfully to integrate environmental, demographic, and health effects models to assist in rapidly reconstructing and visualizing the footprint of a biological release and the effect on the impacted population. The first algorithm permits the GIS software to identify the clustering of

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[*] Siegrist, D.W. (1999), "The Threat of Biological Attack: Why Concern Now?," *Emerg. Inf. Dis.* **5**, 505–508; Stern, J. (1999), "The Prospect of Domestic Bioterrorism," *Emerg. Inf. Dis.* **5**, 517–522; and Tucker, J.B., "Historical Trends Related to Bioterrorism: An Empirical Analysis," *Emerg. Inf. Dis.* **3**, 498–504.

† Kaufman, A.F., M.I. Meltzer, and G.P. Schmid (1997), "The Economic Impact of a Bioterrorist Attack: Are Prevention and Postattack Intervention Programs Justifiable?," *Emerg. Inf. Dis.* **3**, 83–94.

victims in time and space, based on data obtained from simulated interviews of these victims or their family members, once symptoms are recognized. The second algorithm used in the custom GIS application permits the user to select a plume origin that is consistent with a logical estimate of the source strength and height, the location of victim clustering in time and space, and meteorological data for that time and place, and then uses the atmospheric-dispersion algorithm to create a reasonable representation of the plume that accounts for the exposure of the clustered victims, and the entire geographic landscape and population over which it extends, including street networks. Finally, a suitable dose-response model for describing the relationship between dose and infection (and also fatality), is integrated by the GIS software with underlying time-and land-use specific demography to produce a visualization of the impact of the event in terms of expected numbers of infected individuals (and also fatalities) and the time to onset of symptomology for those infected.

Only an analytical system that uses GIS technology can rapidly perform the calculations that identify clusters of victims in time and space from interview data that describe past activities, and then integrate those results with atmospheric-dispersion and dose-response modeling, and related landscape-specific, time-dependent population data to create an infection surface and accompanying statistics for describing the disease and its onset in the impacted population. Furthermore, the custom GIS application is designed to be available to multiple users that would access the system through a secure internet web site using a graphic user interface (GUI), designed specifically for this purpose.

This applied research study required a multidisciplinary team that included environmental scientists, with nationally and internationally recognized backgrounds in meteorology, human-exposure assessment, and human-health-effects risk analysis, as well as computer-software engineers, economists, and geographers with specialized and unique expertise developing and advancing GIS technology. All contributors were from the Health and Ecological Assessment Division in the Earth and Environmental Sciences Directorate of the University of California, Lawrence Livermore National Laboratory.

The technical accomplishments of this research show that more complicated reconstruction of a variety of CUBEs are feasible by further enhancing this prototype-software system, and LLNL is now in a favorable position to make such enhancements. Also, it is apparent that components of this software, particularly the analysis of victim clustering in time and space, are readily and directly applicable to accelerate routine epidemiological investigations performed by state public health agencies and/or the Centers for Disease Control and Prevention (CDC).

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INTRODUCTION

As the United States plays a greater role in the 21st Century as global peacekeeper and international defender of human rights and democratic principles, there is an increasing likelihood that it will become the focus of acts of terrorism. Such acts of terrorism—sometimes described as “asymmetric”—could involve the threat or use of weapons of mass destruction (WMD), particularly those considered unconventional, which include ones designed to release chemical or biological agents. In fact, biological agents are of great concern because, as noted by D.A. Henderson of the Center for Civilian Biodefense Studies at Johns Hopkins University in Baltimore, MD, “… with shortages of hospital space, vaccines, antibiotics, there would be chaos.” (Williams, 2000).

Unfortunately, potential aggressor nations, terrorist groups, and even individuals, can, for a modest cost and effort, develop covert capabilities for manufacturing, transporting, and offensively using biological weapons of mass destruction. Furthermore, there is evidence to indicate that terrorist increasingly are targeting civilian populations—in order to inflict indiscriminate casualties—as well as other more traditional targets such as symbolic buildings or organizations (see Tucker, 1999), which suggest that introducing rapid treatment after a biological event may be more practical than concentrating on prevention (see Siegrist, 1999), especially because sensors are unlikely to be placed in all major urban areas to detect even an atmospheric biological release. For these reasons, and because symptoms for the majority of those effected may not occur or be directly identified for several days, early identification of a covert undetected biological event (CUBE) will contribute to timely medical intervention, which can save many lives.

Specifically, any act of terrorism perpetrated as a CUBE may be more destructive, attract wider attention, and generate greater fear than the use of a chemical weapon that might otherwise have been employed [see Siegrist (1999) and Stern (1999)]. Complicating matters is the fact that a CUBE may be unrecognized initially because of 1) the delay between exposure and the appearance of symptomology, 2) the further delay created by the potential for misdiagnosis of the first patients to present symptoms, because the symptoms are similar to those of other common diseases and most clinicians are unlikely to be familiar with agent-specific symptomology, and 3) the likelihood that victims may report to medical providers at locations scattered throughout the region in which they were exposed. Consequently, recognition of a CUBE in its early stages could be the most effective way to save lives and reduce the cost of the impacts (see Kaufmann et al., 1997). Accordingly, one effective solution is development and implementation of a computerized system of advanced algorithms that will rapidly reveal and reconstruct undetected clandestine releases of biological agents in urban areas that are discovered only after disease symptoms are recognized in one or more victims. The benefits of such a system are to improve the effectiveness of three important first-responders: law-enforcement, whose responsibilities include forensics, attribution, and apprehension of perpetrators; medical providers, responsible for distributing scarce resources, such as antidote, vaccine, and equipment to victims; and recovery managers, who are responsible for risk communication, decontamination, and reentry requirements.

The analysis tool successfully developed for this exploratory research project employs a custom geographic information system (GIS) application and advanced algorithms to assess the consequences of a CUBE by successfully integrating the following data:

1) Baseline geographic and demographic data: street networks, census-block groups, place names, digital phone books, and land uses;
2) Geospatial and temporal details associated with the time-histories of victims diagnosed with symptoms;
3) Archived environmental observations (e.g., meteorological parameters: wind direction, speed, and stability class) pertaining to specific media (e.g., air), and
4) Environmental transport and fate, and dose-response models and their respective parameters.

This integration of data and modeling permits the system to 1) display the convergence (i.e., clustering) in time and space of victims, 2) assist with identifying the likely origin of the release of biological material and show the surface area and corresponding population over which that agent may be dispersed, and 3) reveal graphically the incidence of infection in the population exposed under the plume, as well as provide statistics describing the time-to-onset of the disease in the infected members of the population. Thus a scientifically defensible analysis tool has been created to reconstruct a CUBE reliably and rapidly, following the earliest recognition of symptomology in an exposed population.

The development of the system required a multidisciplinary team of scientists and engineers from the Health and Ecological Assessment Division in the Earth and Environmental Sciences Directorate at the University of California, Lawrence Livermore National Laboratory. Individual contributors possessed nationally and internationally recognized expertise and experience in environmental modeling and human-health effects assessment, as well as unique competencies and capabilities for developing specialized and advanced applications using GIS-software technology.

APPROACH and COMPONENTS

In order to accomplish the stated objective for this study, a reasonable hypothetical scenario was developed that involved an atmospheric release by terrorists of endospores of the gram-positive soil bacteria, *Bacillus anthracis*, onto a city landscape. Anthrax endospores are considered potent as a biological weapon because of their hardiness and dormancy in the environment and ability to express virulence in humans, especially following inhalation (Dixon et al., 1999). The basis for the selected scenario is the accidental release in 1979 of anthrax spores from a secret biological research facility operated by the Russian military in the city of Sverdlovsk (now Yekaterinburg in the Russian Federation) and the epidemic of human anthrax that resulted. Moreover, the source of that event was not determined until Meselson et al. (1994) reconstructed the convergence of victim exposure locations spatially and temporally from interviews with surviving family members, and then performed a retrospective analysis of meteorological conditions for that time when the victim clustering occurred (i.e., April 2, 1979). The steps employed by Meselson et al. (1994) to assess the Sverdlovsk incident serve as a foundation for the more advanced algorithms used with the GIS software for the hypothetical scenario.

System Architecture

The system developed in this exploratory research and development project is an information synthesis and analysis system that employs custom GIS technology to integrate street network, demographic, land use, and victim-history data with atmospheric and dose-response algorithms to rapidly assess and visualize a CUBE. Authenticated users will access the web site hosted at a centrally located server through a graphic user interface (GUI). Users will be able to submit victim-history data, query the system for information, interact with the central processor and GIS analysts, and download results. The system architecture is shown in Fig. 1.

Within the system architecture are two main sections, the GUI and the web-server processes. The user communicates via the GUI with the GIS software and associated dispersion and health-effects algorithms and baseline data and receives system output via the GUI. Closely associated with the GUI is the victim data, gathered from the field, that can be input or edited individually, or transmitted in electronic packages to the Server Center for batch input.

The second area is the GIS web server and process functions that include all the GIS-software modules, the web-server software applications, dispersion model(s), the applicable health-effects models for each biological agent in the library, and other important related functions provided by GIS software and the server center staff. Among other related functions are baseline-data acquisition and input, which must be formatted correctly, subjected to quality control, and edited before it is useful.

Graphic User Interface

Users access the system via a web browser; the GUI, shown in Fig. 2, consists of tab links to pages that include an authentication process, an event page, an analysis page, and a scenario page.

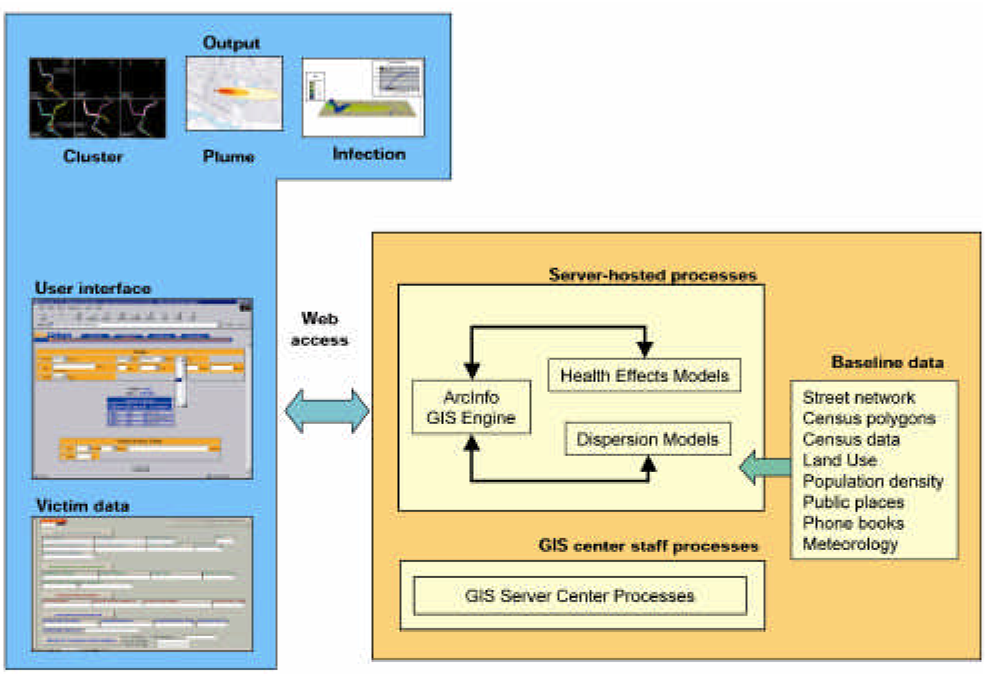

Fig. 1. The system architecture.

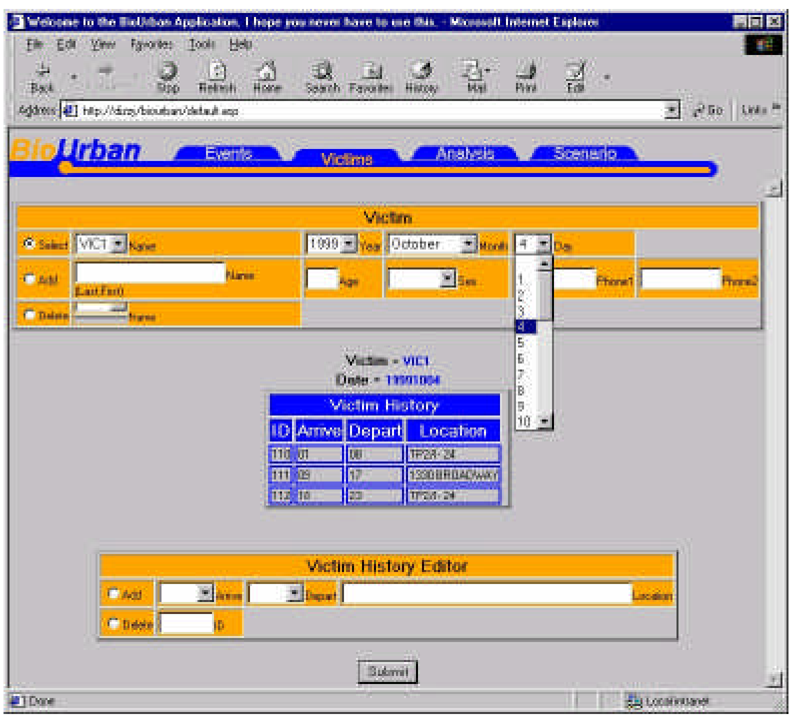

Fig. 2. Graphic User Interface (GUI) for interaction with system.

Hardware and Software Requirements

The system was written using the most recent version of Environmental Systems Research Institute, Inc., (ESRI), GIS software—*ArcInfo™ 8.0* (ESRI, 1999), with GRID, Network, Map Objects, Internet Map Server, and Map Objects 2.0 modules. This software performs all of the geospatial computations. Other functions, including the dispersion algorithm, the dose-response algorithm, and the web-site server system are written in a combination of computer languages, including Visual Basic, FORTRAN, html, and java. This enables users to access and use the system via any web browser on any hardware platform.

The system is designed for deployment on any NT or UNIX server and will be maintained and operated by a team of GIS specialists and applications developers. These individuals will be located at a Server Center and all will be familiar with the ESRI suite of GIS-software modules. Users need only a web browser operating on any hardware platform and authorization to access the system.

Baseline-Data Requirements

Required data include a city street network and meteorological monitoring data (wind speed, direction, stability class). Additional data include topography; geo- and ortho-rectified imagery; the digital yellow- and white-telephone book pages; census-block-group details; land-use and related population-density information; and locations of public places, such as large arenas and auditoriums, prominent public buildings, schools, hospitals, and transit systems. It is necessary for these data sets to be updated, transformed to a common geographic projection, edited, and stored for immediate access on a regular maintenance schedule.

Server Center Staff

The system is designed as a web-based interactive application that authorized users access via an authentication process. Users enter information or edit previously submitted information, request analyses and displays, view the results returned to them, enter more data, and make additional requests. The Server Center staff performs many of the requested analyses using specialized GIS procedures. The staff would also maintain the server hardware and all essential software. During an actual event (or simulation for practice), they will process data, contribute their specialized GIS knowledge to ensure analyses are executed properly and results are returned appropriately over the Internet to authorized users.

Geographic Information System

The custom GIS application executes the integration of the geospatial and temporal input data, and returns analyses and modeling output to the user as projected display images. The primary GIS processes and concepts are discussed below.

CUBE Geographic Study Area and Transfer Points

As initial victim time-history data come into the service center and clustering is revealed, a subjective judgment of the geographic area of the release is made by the staff in order to begin providing output and to limit data processing requirements. A study area, shown in Fig. 3, is approximately 10 to 15 mi^2 and bounds the likely exposure area. Once a study area is defined, geographically referenced street data are incorporated from the baseline data to serve as the fundamental landscape of the analyses to follow.

The study area concept also includes the concept of “transfer points,” both on the perimeter of the study area rectangle (representing ground travel out of the study area) and at airports, train stations, bus depots, or ports, that represent victims’ geographic location of ingress or egress with respect to the study area of interest (see Fig. 3). The study area and transfer points function as follows: assume, that for a given day, interview data show a victim was at work in an urban area from 08:00 through 17:00, then the victim traveled 35 miles, arriving at home 18:00, where he stayed until driving back to the city between 07:00 and 08:00 the next day. The victim then boarded an airplane at 14:30 for New York on the second day. Assuming the event took place in the vicinity of the individual’s work location, a transfer point is assigned at the appropriate intersection of the study-area boundary with the route of ingress or egress (e.g., by auto, or metropolitan transit system) to and from home. Another transfer point is assigned at the airport to account for the victim’s leaving (and perhaps reentering) the vicinity of the CUBE from that location. The whereabouts of the victim in distant locations may later prove important to the investigation, but for the moment does not contribute to the complex geospatial and temporal calculations required to identify clusters of victims inside the selected study area. The transfer-point concept accelerates and facilitates GIS computation and enables results to be returned to users more rapidly.

The Statistical City Database

In addition to locating the common whereabouts of victims, it is necessary to know the demography of the vicinity of the CUBE at the time of the release. The system includes a method to estimate the population density of any of several different land use types: residential; commercial; industrial; open space; park; aquatic; unoccupied grazing, farm, crop, forest, or preserve; and special-event areas, such as coliseums. Available data describing population densities is associated with each of the land use types for a specific time block. When the dispersion algorithm generates a plume grid, that grid is intersected with the corresponding GIS polygons (i.e., cells) that contain specific land-use and population information for the time of day and location over which the plume spread; the population affected in any given cell is determined by the ratio between population density and area covered by the plume.

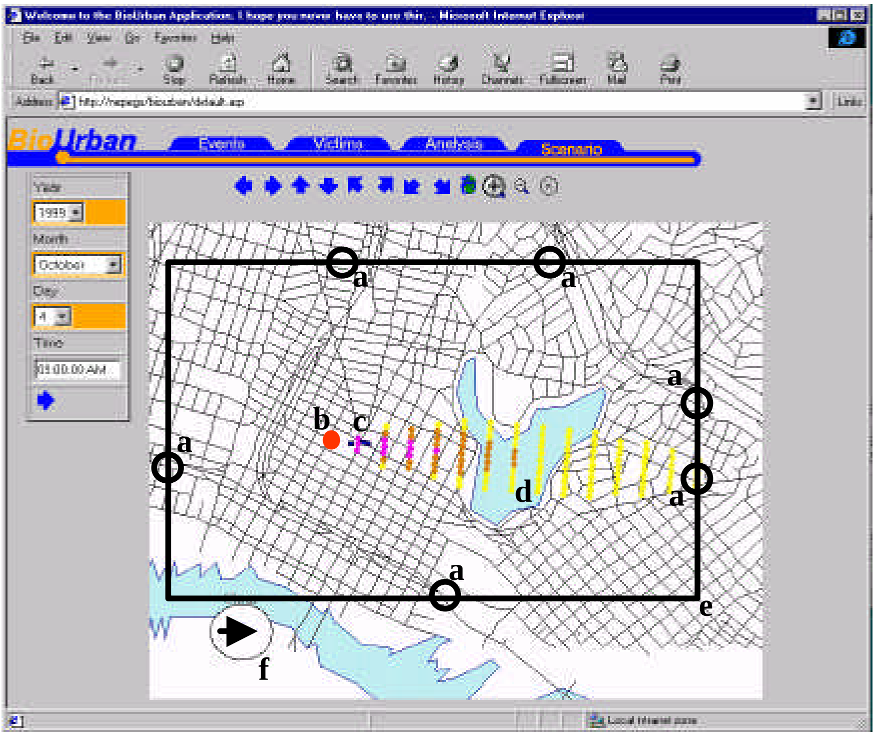

Fig. 3. Display of CUBE study area: a) transfer points, b) plume origin, c) victim cluster, d) preliminary representation of dimensions of plume footprint, e) study-area boundary, and f) wind rose corresponding to time and location of victim cluster.

Victim Data Collection, Processing, Geocoding, and Network Analysis

Reconstructing a CUBE requires data on the whereabouts of each victim over several days prior to onset of diagnosed symptoms. To gather such information, a data form was developed that organizes time and location elements necessary to recreate the activities of victims that occurred in the recent past—where they were, and when they arrived at and departed from specific locations. This form and the approach used are compatible with the relational database system of data collection and archiving used by the Federal Bureau of Investigation (FBI).

Sever Center staff then process the victim data. Each location of each victim is address matched, a GIS process that assigns a geocoordinate location from street address or other information describing each stationary or travel-route location of each victim.

Then, the GIS software is used by the staff to perform a network analysis, which fills in the routes between points in a victim's past schedule. Thus, the system creates points and route lines corresponding to all or nearly all the time blocks of each victim over the time period under consideration (e.g., 10 days prior to onset of symptoms). These are color coded by time block for easy identification by users.

Output

The result of the GIS server-center procedures, calculations, and algorithms is a series of outputs that help the user understand the events and implications related to a terrorist CUBE. The primary outputs are shown in Figs. 4, 5, and 6 and are discussed below.

The first output delivered from the server to users is a color-coded display of lines and points representing locations by time block of all known victims. This is shown in Fig. 4 as a cluster analysis. Using this color-coded display, any clustering in time and space among victims can easily be identified. The panels can represent 24-hour, 12-hour, or 4-hour sets of time increments. The user observes color clustering. If all or nearly all of the victims appear to be clustered in the same space in the same time block, as shown in one of the color-coded panels, the user then selects this panel and moves to the Scenario window for further detailed analyses.

The Scenario page enables users to estimate the origin point and footprint of a plume associated with a CUBE. The Scenario page displays a detailed map of the streets in the study area and the victims' locations during the time block selected in the Scenario panel. A wind rose (obtained from archived meteorological data) is also displayed showing wind direction for the time and location of clustering. The user estimates an origin point for a plume, and its likely characteristics, including estimated source strength. The atmospheric-dispersion code returns a plume based on the meteorological data for the estimated time of the release (refer to Fig. 5).

The system service center oversees the processing of the selected plume dimensions together with the time-dependent population in the vicinity. The products of this effort are an accurate representation of the infectivity surface and the statistics describing the time-to-onset of disease for the infected members of the population. This output is shown Fig. 6.

As part of this project, we have created a document describing procedures the Server Center staff will use to locate, read in, and edit the important baseline data that is readily available and relatively uniform in extent, precision, accuracy, projection, and other factors for all major metropolitan areas in the US. It is assumed that the GIS Server Center staff will be very experienced in GIS technology, development, and applications.

Atmospheric-Dispersion Modeling

For purposes of this study and the hypothetical scenario selected, a simple Gaussian-plume model was used to determine a reasonable source term (total spores released) for an atmospheric release of anthrax spores into an urban environment. The model used is similar to the one described by Meselson (1995) for reconstructing the Sverdlovsk incident, and assumes the source would also be at 10 m and produce similar centerline doses downwind for an urban environment to those doses calculated downwind for Sverdlovsk. Then this source characterization was used in the VLSTRACK atmospheric-dispersion model (Bauer and Gibbs, 1997), along with sampled meteorological data that was assumed to correspond to the hypothetical time of release.

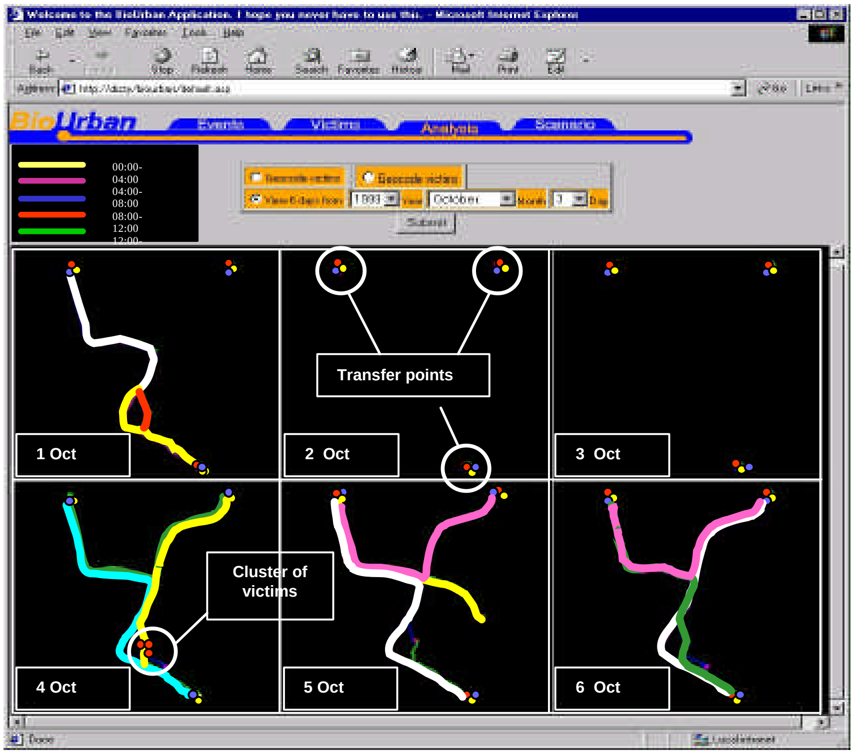

Fig. 4. Output of cluster analysis (derived from victim interviews; see also Fig. 1).

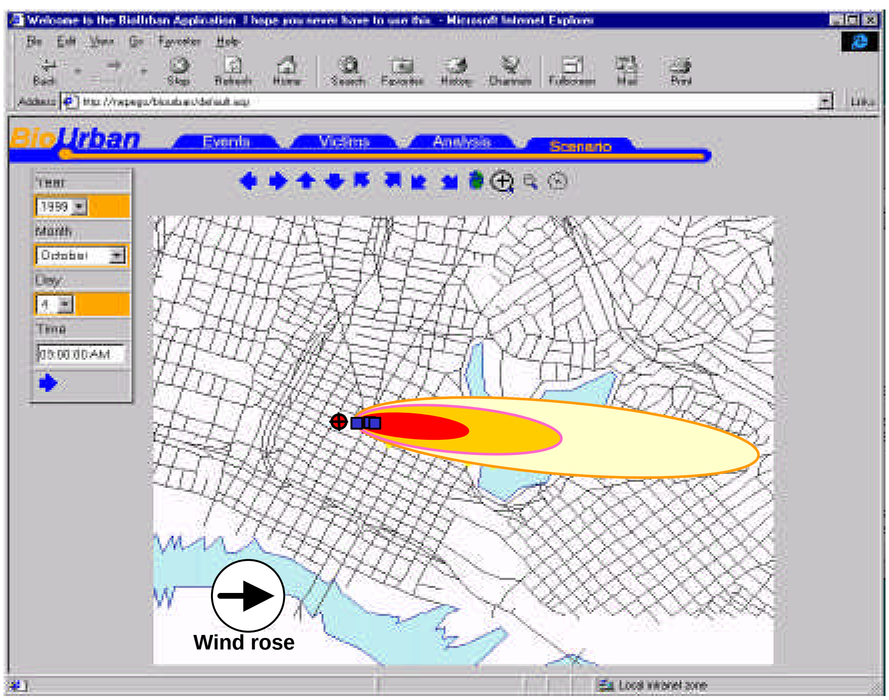

Fig. 5. Output of plume origin and footprint (consistent with reasonable estimate of source strength, and victim-cluster location and time; see also Fig. 1).

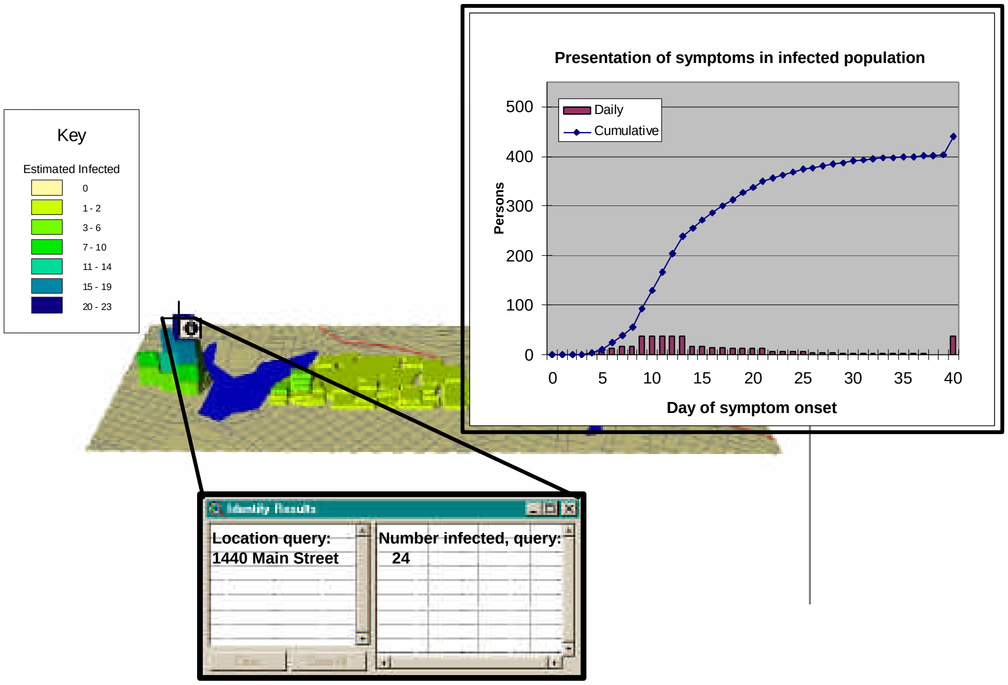

Fig. 6. Output of infectivity surface and statistics describing time-to-onset of symptoms in infected population (determined from integration of results of atmospheric dispersion and dose-response modeling with detailed information on land-use and population demographics under the plume footprint; see also Fig. 1).

To select a reasonable source term for the plume in terms of breathing-height exposure to anthrax spores for a scenario involving the release of *B. anthracis* from a stationary source into the air of an urban environment, Eq. 1 is used (see Hanna et al., 1982) :

$$Q = \frac{D\left(\pi\, u\, \sigma_y\, \sigma_{\Delta h}\right)}{B\left[e^{-\frac{1}{2}\left(\frac{y}{\sigma_y}\right)^2} e^{-\frac{1}{2}\left(\frac{\Delta h}{\sigma_{\Delta h}}\right)^2}\right]}, \qquad (1)$$

where

Q = total number of anthrax spores released at the source [2.4×10^{10} spores was used because it provides similar inhalable doses of anthrax spores to those generated by Meselson (1995) along a plume centerline for a 5 m/sec wind speed and 10 m release height];

D = dose, represented by number of anthrax spores inhaled (e.g., approximately 20 spores for the centerline dose at a downwind distance of approximately 3 km);

B = breathing rate (assumed to be 0.03 m^3/sec) for an exposed individual engaged in light work (see Meselson, 1995);

π = constant (3.14);

u = wind speed (i.e., considered to be 5 m/sec) at height of release (assumed to be 10 m), based on data reported by Meselson (1995);

s_y = horizontal-plume spread, $0.16x(1+0.0004x)^{-\frac{1}{2}}$ (for an urban environment and neutral stability), where x (m) is distance downwind;

$s_{\Delta h}$ = vertical-plume spread, $0.14x(1+0.0003x)^{-\frac{1}{2}}$ (for an urban environment and neutral stability), where x (m) is distance downwind;

y = crosswind distance (m), where y is equal to 0 at centerline of plume; and

Δh = considered to be 8 m, which is the difference between the release height (considered to be 10 m) and the breathing-zone height at the receptor (assumed to be 2 m).

The VLSTRACK model was then employed with the source term characteristics derived from above and similar meteorological data as that reported by Meselson (1995) for the Sverdlovsk incident (i.e., 5 m/sec wind speed, and neutral stability). The VLSTRACK model was developed by the US Naval Surface Warfare Center in Dahlgren, VA, for the Office of Naval Technology, in the US Department of Defense, and was designed for operation on the current generation of personal computer platforms with standard operating systems (Bauer and Gibbs, 1997). This model possesses a library of reasonably well described source terms that address the release mechanisms and relevant physical properties for a number of chemical agents, and some significant biological agents, such as anthrax.

The operation and output of VLSTRACK are well described and transparent to the experienced user of such models and can be readily assimilated without much difficulty by other software systems, such as the custom GIS application. Additionally, time-varying meteorological monitoring data collected routinely by surface monitoring stations can be used by VLSTRACK for describing plume behavior and breathing height concentrations of released substances. Although VLSTRACK is limited because it does not currently account for effects of terrain features (e.g., individual obstacles, such as a building or a hill or tree line), it does account for terrain characteristics (e.g., water, sand, grass, forest, etc.).

A computational process was devised to properly transform the grided output data from VLSTRACK for implementation by the custom GIS application. This procedure permitted the grided format to be incorporated and used by the GIS software to generate contours of equal dose (i.e., inhaled spores), positioned on a data-rich landscape surface, and then visualized geospatially.

Other atmospheric-dispersion models could be used, even one as simple as that described by Hanna et al. (1982), however, VLSTRACK was attractive for purposes of this project for three important reasons. First, it is easily implemented on desktop computer platforms, and can rapidly produce adequate approximations of contours of inhalable spores. Second, its operation and output are well described, accepted, understood, and transparent, and its outputs can be readily assimilated and transformed without much difficulty. Third, meteorological monitoring data collected routinely by surface monitoring stations (and archived for later use) can easily be used by the VLSTRACK model for describing plume behavior and producing breathing-height contours of dose for released substances. Although VLSTRACK and simple models are somewhat limited because they do not account very well for effects of individual terrain features on atmospheric dispersion, they are still suitable for use in most relatively flat environments, and they can be employed to provide useful results rapidly.

Health-Effects Analysis

The health-effects analysis component of the system consists of two scientifically plausible mathematical algorithms. The first one identifies either the percentage of the population likely to be infected or likely to suffer fatality following exposure to anthrax spores by inhalation. The second algorithm yields the time to onset of symptoms for those infected. The custom GIS application applies these algorithms to the plume contours of dose of inhaled spores and the census demography under the plume in order to quantify the infected number of individuals in the population on the geographic surface over which the plume has dispersed. Such modeling of health effects (including both infection and mortality), and not just fatality exclusively, for exposed individuals constitutes a major new enhanced capability for decision makers confronted with administering medical intervention to prevent fatality, and performing cleanup.

To facilitate the goal of demonstrating this capability, it was necessary for the exposed population to be considered homogeneous. Accordingly, the exposed population was considered to be in good health, performing moderate activity at the time of exposure, and with no prior exposure to the released organism. Also, only inhalation exposure is addressed in this scope of work. Nevertheless, this effort illustrates that it is reasonable for further advances to be made to the system to improve how it addresses consequences for different populations of individuals (e.g., including children, the elderly, and immunocompromised, as well as those with different activities), and perhaps even multiple exposure pathways, such as ingestion, as well as inhalation.

The approach for performing the infection analysis involves using a lognormal dose-response model that relates inhaled dose for anthrax to mortality, and by adjustment to infection. This model was described by Meselson et al. (1994) and Meselson (1995) for mortality, and adjusted to also address infection, using additional data from Sverdlovsk. The lognormal relationship was selected because it best reflects heterogeneity in susceptibility in the exposed population (Meselson, 1995). The relationship between inhaled spores (i.e., dose of *B. anthracis*), and subsequent infection is expressed mathematically in Eq. 2.

$$P_{\mathrm{Inf}} \quad = \quad \frac{\Phi\left[\left(\log D - \log LD_{50}\right) f\right]}{n}, \tag{2}$$

where

P_{Inf} = the cumulative percentage (%, when expressed as $100 \times P_{\mathrm{Inf}}$) of infected individuals in a human population exposed to anthrax spores released into the air of an urban environment. In this case, $\Phi(z_{\mathrm{p}})$ yields $0 \le p \le 1$ for the standard normal deviate $-8 \le z \le +8$);

D = dose, expressed as total number of anthrax spores inhaled (i.e., obtained from atmospheric-dispersion model data for specific locations under the plume);

LD_{50} = estimated median lethal dose for humans for inhaled anthrax spores (i.e., 8000 spores; or log LD_{50} = 3.9), based on US Department of Defense data described by Meselson et al. (1994) and Meselson (1995);

f = the probit slope (i.e., 0.7 probit per log dose), obtained from a large-scale inhalation anthrax experiment performed using primates (cited by Meselson et al., 1994);

n = fraction of infected individuals likely to suffer mortality (i.e., 0.9), based on data for the pipe shop workers in Sverdlovsk following inhalation exposure to anthrax (see Meselson et al., 1994; and Meselson, 1995). Note, if n is not used in Eq. 2, then Eq. 2 generates only the cumulative percentage of mortality expected in the population exposed to anthrax by inhalation.

Consequently, for any given dose predicted by the atmospheric-dispersion model for a particular location under the plume, Eq. 2 can estimate the percentage of the population at that exposure point that would be infected. Combining this result with the demographic data for that location available in the GIS database, yields a value for the number of infected individuals at that location. This information can be displayed three dimensionally as an infection surface on the geographic landscape underlying the plume contours. Now medical providers and resource-recovery authorities can use this surface to more easily determine the location of the highest density of infected individuals and the extent of the entire plume footprint.

For anthrax exposure, not only is it important to approximate the plume footprint, and to estimate the total number of people infected and even the total number of fatalities as a result of the release, but it is also crucial for first responders and decision makers to know the time when a given fraction of those exposed are likely to present their symptoms. This information is vital because only the administration of medical therapy, particularly antibiotics, and perhaps even supportive procedures (e.g., assisted ventilation to maintain airway competency), just prior to symptom onset from anthrax infection or very soon thereafter, can save the lives of those infected and prevent a mortality rate of nearly 100 percent by health-effects such as severe respiratory distress, cyanosis, and shock (NRC, 1999; and Dixon et al., 1999).

To estimate the relationship between the day symptoms begin and the estimated cumulative percentage of infected individuals presenting symptoms on that day, a log-probability plot was constructed of the time to onset of anthrax symptoms for the victims of the Sverdlovsk incident, based on the case data reported by Meselson et al. (1994). The plotted points lie approximately on a straight line, which suggests these data are from a normal distribution. The best-fitting straight line through the plotted points was computed and used to describe analytically the relationship between the days to onset of symptoms after exposure and the cumulative percentage of the infected population likely to express symptoms on or before that day. Thus the cumulative percentage of individuals in the infected population likely to be symptomatic on or before time *t*, expressed in days after exposure, can be determined using Eq. 3.

$$P_{\text{Onset}} = \Phi\left[\frac{\ln\left(\frac{t}{14.368}\right)}{0.61604}\right], \tag{3}$$

where

P_{Onset} = the cumulative percentage (%, when expressed as $100 \times P_{\text{Onset}}$) of infected individuals expressing symptoms of inhalation anthrax on or before time *t* (days). In this case, $\Phi(z_{\text{p}})$ yields $0 \le p \le 1$ for the standard normal deviate $-8 \le z \le +8$); and

t = time to onset of symptoms (d) for individuals in the infected population.

The percentage, P_{Onset}, can now be applied to any part of the infection surface or the entire surface itself, for any specific day after the event, to determine the number of infected people likely to present symptoms on that particular day. As the case data presented by Meselson et al. (1994) shows for Sverdlovsk, onset could range from as early as 4-d post exposure to more than 40 d (median estimated to be 14 d). This information can be used by medical providers to predict how many infected people will need services on any given day after the event, and how many could be past the “point of no return” and would not necessarily be helped by any medical intervention. This information can have dramatic implications for distributing scarce resources (e.g., antibiotic, hospital beds, and ventilators) in order to maximize the number of lives that can be saved, and even to prepare for handling fatalities.

TECHNICAL ACHIEVEMENTS AND CONCLUSION

The major technical achievement produced by this multidisciplinary effort was to successfully demonstrate a web-accessible custom GIS application that can help identify the location and time of a CUBE involving the airborne release of anthrax spores into an urban environment. The GIS application integrates victim time and location information, underlying time- and land-use sensitive demographic information, atmospheric-dispersion modeling, and the relevant dose-response function. This data integration allows the system to assist users in locating the plume and identifying the population underlying—and therefore exposed to—the plume and estimate the probable health consequences to this exposed population. Such information can then be used to save lives and limit costs.

These results were possible because the GIS application can quickly generate a picture on a geographically accurate landscape of 1) the geospatial and temporal convergence of the exposed population, based on assimilation of time-history data obtained about victims known to be infected; 2) contours of inhalation dose for anthrax spores released into air and dispersed over an urban landscape for a specifically positioned and characterized source term, based on atmospheric-dispersion modeling; and 3) the impacts on the exposed population in terms of infection, mortality, and time to onset of symptoms, based on the exposure pathway (e.g., inhalation) and dose-response modeling for the exposed individuals present on the geographic landscape during plume passage. Indeed, the capability to model health effects (including both infection and mortality), and not just fatality exclusively, for exposed individuals constitutes a major new enhanced capability. These details will provide to law-enforcement personnel a reasonable location to begin sampling for evidence, to medical providers information essential for distributing scarce resources for saving lives and limiting costs, and to resource-recovery managers particulars concerning the likely extent of contamination that can be used for specifying requirements for allowing reentry, performing cleanup, and communicating risks.

In conclusion, the results of this project clearly demonstrate that a web accessible interactive GIS application can integrate atmospheric-dispersion and dose-response models to provide timely information to accelerate the process of identifying and effectively responding to a CUBE that involves the atmospheric release of a biological agent into an urban environment. It also shows that such a system has the potential for accelerating epidemiological investigations of outbreaks of food poisonings, or infectious diseases, because of its ability to rapidly decipher geospatial and temporal information on victim activity patterns. Accordingly, this system has the potential not only to be deployed for use in a CUBE, but to have components, such as victim clustering analysis, applied routinely for accelerating epidemiological investigations, including those focused on determining the sources of unusual emerging infectious diseases [e.g., West Nile virus outbreak in New York City, NY (Schoch-Spana, 1999)]. In both applications, the results would improve the opportunity for decision makers to intervene in a more timely manner than is now possible for such events and in so doing more quickly identify the source, reduce or prevent illness, and contain costs.

Future Developments

Advances and enhancements to the system that can be made in the future include: 1) adding dispersion codes that address atmospheric-flow complexities in urban environments more quantitatively, 2) incorporating methods to more efficiently identify clustering of victims, 3) providing algorithms to improve user estimates of plume origin, 4) increasing the library of possible biological threat agents and their corresponding dose-response algorithms, 5) developing dose-response algorithms that include the effects of sheltering, varying susceptibilities to infection in the population, 6) improving data on land use and population densities, 7) providing capabilities for optimizing sensor placement and acquisition of real-time sensor data (both of which were developed in a previous project and may be applicable in the future for this system), and 8) continuing to optimize overall system performance. The technical achievements accomplished in the development of this system place the Lawrence Livermore National Laboratory in a favorable position to make these advances and enhancements in the future.

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